

Study links frequent red meat consumption to high levels of chemical associated with heart disease

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Researchers have identified another reason to limit red meat consumption: high levels of a gutgenerated chemical called trimethylamine N-oxide (TMAO), that also is linked to heart disease. Scientists found that people who eat a diet rich in red meat have triple the TMAO levels of those who eat a diet rich in either white meat or mostly plantbased proteins, but discontinuation of red meat eventually lowers those TMAO levels.

TMAO is a dietary byproduct that is formed by gut bacteria during digestion and is derived in part from nutrients that are abundant in red <u>meat</u>. While high saturated <u>fat levels</u> in red meat have long been known to contribute to <u>heart disease</u>—the leading cause of death in the United States—a growing number of studies have identified TMAO as another culprit. Until now, researchers knew little about how typical dietary patterns influence TMAO production or elimination.

The findings suggest that measuring and targeting

TMAO levels—something doctors can do with a simple blood test—may be a promising new strategy for individualizing diets and helping to prevent heart disease. The study was funded largely by the National Heart, Lung, and Blood Institute (NHLBI), part of the National Institutes of Health. It will be published Dec. 10 in the *European Heart Journal*, a publication of the European Society of Cardiology.

"These findings reinforce current dietary recommendations that encourage all ages to follow a heart-healthy eating plan that limits red meat," said Charlotte Pratt, Ph.D., the NHLBI project officer for the study and a nutrition researcher and Deputy Chief of the Clinical Applications & Prevention Branch, Division of Cardiovascular Sciences, NHLBI. "This means eating a variety of foods, including more vegetables, fruits, whole grains, low-fat dairy foods, and plant-based protein sources such as beans and peas."

"This study shows for the first time what a dramatic effect changing your <u>diet</u> has on levels of TMAO, which is increasingly linked to heart disease," said Stanley L. Hazen, M.D., Ph.D., senior author of the study and section head of Preventive Cardiology & Rehabilitation at the Cleveland Clinic. "It suggests that you can lower your heart disease risk by lowering TMAO."

Hazen estimated that as many as a quarter of middle-aged Americans have naturally elevated TMAO levels, which are made worse by chronic red <u>meat consumption</u>. However, every person's TMAO profile appears to be different, so tracking this chemical marker, Hazen suggested, could be an important step in using personalized medicine to fight heart disease.

For the study, researchers enrolled 113 healthy men and women in a clinical trial to examine the



effects of dietary protein—in the form of red meat, white meat, or non-meat sources—on TMAO production. All subjects were placed on each diet for a month in random order. When on the red meat diet, the participants consumed roughly the equivalent of about 8 ounces of steak daily, or two quarter-pound beef patties. After one month, researchers found that, on average, blood levels of TMAO in these participants tripled, compared to when they were on the diets high in either white meat or non-meat protein sources.

While all diets contained equal amounts of calories, half of the participants were also placed on high-fat versions of the three diets, and the researchers observed similar results. Thus, the effects of the protein source on TMAO levels were independent of dietary fat intake.

Importantly, the researchers discovered that the TMAO increases were reversible. When the subjects discontinued their <u>red meat</u> diet and moved to either a white meat or non-meat diet for another month, their TMAO levels decreased significantly.

The exact mechanisms by which TMAO affects heart disease is complex. Prior research has shown TMAO enhances cholesterol deposits into cells of the artery wall. Studies by the researchers also suggest that the chemical interacts with platelets—blood cells that are responsible for normal clotting responses—in a way that increases the risk for clot-related events such as <u>heart</u> attack and stroke.

TMAO measurement is currently available as a quick, simple blood test first developed by Hazen's laboratory. In recent published studies, he and his colleagues reported development of a new class of drugs that are capable of lowering TMAO levels in the blood and reducing atherosclerosis and clotting risks in animal models, but those drugs are still experimental and not yet available to the public.

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